REMARKS

Claims 4 and 8 remain rejected under 35 U.S.C. §103 as obvious over Desmyter taken with Yano 1, Bever and Liaw, further in review of Yano 2. Applicants respectfully traverse this rejection.

The claimed invention relates to a method of treating hepatitis C using a cationic liposome consisting essentially of 2-O-(2-diethylaminoethyl) carbamoyl-1,3-O-dioleoylglycerol and a phospholipid, with a 100-500 bp poly(I):poly(C) in a dosage of 1μg to 50 mg/man per dose. This invention is not taught by any combination of art cited by the Examiner.

In support of the fact that none of the cited references disclose or suggest the presently claimed invention, Applicants submit herewith Declarations under 37 CFR §1.132 by Kazuko Hirabayashi (hereinafter the "Hirabayashi Declaration") and Junichi Yano (the "Yano Declaration").

To appreciate the present invention, a review of the art at the time the present invention was made is helpful. At that time, it was known that poly(I):poly(C) could induce interferon in vivo, and that interferon was effective in treating hepatitis. (Hirabayashi Declaration at ¶5) It was also known, however, that poly(I):poly(C) could not be used as a medication due to the fact that commercially available poly (I):poly(C) (unshortened poly(I):poly(C)) had a strong toxicity even though it could induce a sufficient plasma level of interferon and that the shortened poly(I):poly(C) such as a 100-500 bp poly (I): poly(C) only weakly induced interferon in vivo. Id. Indeed, even Yano 1, cited by the Examiner, notes the "strong toxicity" problem with poly(I):poly(C). Yano

1 at col. 3, lines 41-50. For these reasons, at the time the present invention was made, a person of ordinary skill in the art would not have considered poly(I):poly(C) to be useful as a medicine. (Hirabayashi Declaration at ¶¶5, 13 and 14, Yano Declaration at ¶¶8, 9)

It is in this context the inventors found, for the first time, that a specific combination of the 100-500 bp poly(I):poly(C), with a specific carrier comprising 2-O-(2-diethylaminoethyl) carbamoyl-1,3-O-dioleoylglycerol and a phospholipid was useful in treating hepatitis C in humans because this specific combination induces a sufficient plasma concentration of interferon in vivo for treating hepatitis C, and it has very low toxicity. Nothing in the prior art teaches or even remotely suggests such an invention. Moreover, the inventive combination induces high, and probably higher, concentrations of interferon in the liver, because the inventive combination accumulates in the liver. See Specification at page 3, Fig. 1 and Fig. 2. (Hirabayashi Declaration at ¶¶7, 8, 9)

Turning to the references cited by the Examiner, Desmyter does not even relate to treating hepatitis C in the first instance. Rather, Desmyter only discusses hepatitis B. The fact that hepatitis B and hepatitis C are different in their responsiveness to interferon is beyond dispute. (Hirabayashi Declaration at ¶18) Even the Liaw reference, relied upon by the Examiner, notes the differences between hepatitis B and hepatitis C. (Hirabayashi Declaration at ¶¶18 and 20)

Moreover, Desmyter does not disclose administering poly(I):poly(C), let alone the 100-500 bp poly (I): poly (C), complexed with the cationic liposome consisting essentially of 2-O-(2-diethylaminoethyl) carbamoyl-1,3-O-dioleoylglycerol and a phospholipid. (Hirabayashi Declaration at ¶17)

Finally, Desmyter uses a dose of 3 mg/kg. This is far higher than the claimed dose, and in fact the Desmyter dose is probably toxic. (Hirabayashi Declaration at ¶¶9, 18)

Yano 1 does not cure the defects of Desmyter. First, Yano 1 does not even mention hepatitis. Thus, it does not cure the defect in Desmyter of failing to mention hepatitis C. Moreover, Yano 1 does not relate to poly(I):poly(C). Rather, it relates to the usage of a mismatched RNA (a part of $-NH_2$ groups substituted with –SH) as an interferon inducer. Yano 1 at claims 1-3. (Hirabayashi Declaration at ¶15, Yano Declaration ¶¶10-12) Thus, Desmyter's failure to disclose poly(I):poly(C) complexed with the cationic liposome of the claimed invention with a phospholipid cannot be cured by Yano 1. Indeed, Yano 1 does not disclose the cationic liposome of the claimed invention. Id. Moreover, Yano 1 does not overcome the dosage problem of Desmyter. It cannot, since it does not even relate to poly(I):poly(C) in the first instance.

Bever cures none of the defects of Desmyter or Yano 1. First, Bever does not even relate to treating hepatitis. Rather, it relates to treating multiple sclerosis. Second, Bever does not even use poly(I):poly(C), let alone the 100-500 bp poly(I):poly(C). It used Poly ICLC. Third, it does not disclose a complex with the cationic liposome of the presently claimed invention containing a phospholipid. (Hirabayashi Declaration at ¶19)

Contrary to the Examiner's assertion, Liaw actually teaches away from the claimed invention. Specifically, throughout the reference, and particularly at the Abstract and page S351, Liaw teaches that treatment of hepatitis C with interferon, even at higher doses for longer periods of time, is "still not satisfactory". (Hirabayashi Declaration at

¶20) Thus, the Examiner's contention that inducing interferon production equals effective hepatitis C treatment in humans (Office Action at page 4) is simplistic.

As for the remainder of Liaw, it does not teach poly(I):poly(C), let alone the 100-500 bp poly(I):poly(C), cationic liposomes, complexes of poly(I):poly(C) with cationic liposomes, or these complexes having phospholipid. Id.

Finally, Yano 2 does not cure the defects found in the other cited prior art. Like Desmyter, Yano 1 and Bever, Yano 2 does not mention treating hepatitis C. (Hirabayashi Declaration at ¶16) Indeed, it does not even mention treating hepatitis. Moreover, while Yano 2 discloses the cationic liposome of the present invention, it does not teach the specific combination of the cationic liposome of the present invention with poly(I):poly(C). Yano 2 makes no mention of the 100-500 bp poly(I):poly(C). (Yano Declaration ¶13)

Based on the results shown in the Hirabayashi Declaration and the specification at Test Example 3, Applicants respectfully submit that the composition of the present invention (having critical composition of 100-500 bp poly(I):poly(C), with a specific carrier comprising 2-O-(2-diethylaminoethyl)carbamoyl-1,3-O-dioleoylglycerol and a phospholipid) has surprising and unexpectedly superior interferon-inducing properties in vivo with low toxicity when compared to the known compositions at the time the invention was made, and is thus useful for the treatment of hepatitis C. Further, one skilled in the art would not arrive at the presently claimed invention based on the combined teachings in Desmyter, Yano 1, Yano 2, Bever and Liaw.

Accordingly, Applicants respectfully submit the present claims are unobvious over any of the prior art cited by the Examiner (individually and in combination) and respectfully request that the rejection under §103 be withdrawn.

AUTHORIZATION

If the Examiner believes that issues may be resolved by telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 801-2134. The undersigned may also be contacted by e-mail at diebnerg@gtlaw.com.

A three month extension of time fee of $1,020.00 is believed to be necessary. The Commissioner is hereby authorized to charge that fee, and any additional fees which may be required for this amendment, or credit any overpayment to Deposit Account No. 50-1561.

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By: Respectfully submitted,

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